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10/563,785	04/25/2006	John Nolting	PA1394	2982

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EXAMINER	
HELM, CARALYNNE E	

ART UNIT	PAPER NUMBER
1615	

NOTIFICATION DATE	DELIVERY MODE
04/29/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/563,785	NOLTING, JOHN	
	Examiner	Art Unit	
	CARALYNNE HELM	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 January 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,7-12,14,15 and 18-32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3, 7-12, 14-15, and 18-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

NEW REJECTIONS

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 30-32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The disclosure as filed does not provide written basis for the new limitation that the plurality of therapeutic agents is released from the plurality of therapeutic coatings after the adjacent overlying timing coating has completely eroded." Specifically the requirement fro complete erosion was not described; therefore this recitation constitutes new matter.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

The four factual inquiries of Graham v. John Deere Co. have been fully considered and analyzed in the rejections that follow.

Claims 12, 14-15 and 18-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Miller et al. (previously cited) in view of Sirhan et al. (US Patent No. 6,471,980 – henceforth Sirhan et al. reference C).

Miller et al. teach medical devices with a set of layers on their surface that can each contain a different bioactive (see abstract and paragraph 55; instant claim 12). In particular, Miller et al. envision coronary stents as medical devices within their invention (see paragraph 92; instant claim 12). One of ordinary skill in the art at the time of the invention would have found it obvious to select a particular set of therapeutic agents pertinent to the body region treated by the device (e.g. coronary artery). Therapeutic agents considered by Miller et al. are taught to include paclitaxel, dexamethasone, and non-steroidal anti-inflammatory agents (see paragraphs 45 and 49; instant claims 14-15). These therapeutic containing layers are also taught to be composed of

biodegradable (bioerodible) polymers (see paragraphs 40-41; instant claim 13). Miller et al. also teach that the layers are applied to any portion of the device, thus it also would have been obvious to apply them to the full length of the device (which includes the distal, proximal, and mid-portions) (see paragraph 50; instant claims 12 and 19-20). The layered configuration contains a plurality of barrier layers (timing coatings) and a plurality of therapeutic agent containing layers that alternate on the surface of the device (see paragraph 62; instant claim 16). These barrier layers are taught to impede the release of therapeutic agents from the device (see paragraph 56; instant claim 18). Embodiments are envisioned where a barrier layer (timing coating) covers each of three therapeutic agent containing layers (see paragraph 62; instant claims 12 and 20). Miller et al. teach that the layered configuration allows different release profiles of different bioactive agents and can be optimized based upon the desired application (see paragraph 55). The barrier layers (timing coatings) are also taught to be composed of biodegradable polymer and in these instances degradation of the layers controls release of the drug (see paragraphs 32 and 58; instant claims 7 and 12). In view of these teachings, it would have been obvious to one of ordinary skill in the art at the time of the invention to employ bioerodible polymers in the barrier layers and the therapeutic containing layers of Miller et al. Although optimization of the release profile of the contained bioactives is taught, Miller et al. do not explicitly teach sequential release.

Sirhan et al. reference C teaches stents with multiple polymeric coating layers (see column 5 lines 35-62). Classes of drugs also taught present in the coatings of Miller et al. are taught by Sirhan et al. reference C (see column 6 lines 23-29). In

addition, Sirhan et al. reference C teaches separate coating layers with individual drugs in each that are released sequentially, as opposed to simultaneously or both sequentially and simultaneously (see example 7; instant claim 1).

Since Sirhan et al. reference C teaches that it was desirable to provide sequential delivery of combinations of drugs with anti-proliferative, anti-thrombin, and immunosuppressive properties from a series of coatings, and Miller et al. teach optimization of the release profiles of similar classes of compounds from their layered coating, it would have been obvious to one of ordinary skill in the art at the time of the invention to configure the layered coating of Miller et al. such that the drugs were released sequentially (one at a time). Therefore claims 12, 14-15, and 18-20 are obvious over Miller et al. in view of Sirhan et al. reference C

Claims 1-3, 7-12, and 19-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Miller et al. in view of Sirhan et al. reference C as applied to claims 12, 14-15, and 18-20 above, and further in view of Sirhan et al. (previously cited – see IDS - referred to henceforth as Sirhan et al reference B) and as evidenced by Fischell et al. (previously cited).

Miller et al. Sirhan et al. reference C make obvious a coronary stent with alternating barrier layers (timing coating) and therapeutic agent containing layers that all contain bioerodible polymers and are arranged such that the distal and proximal ends have a plurality of each while the mid-portion has at least one of each. In addition, the claimed therapeutic agents, release kinetics (sequential release) and presence of

bioerodible polymers in each layer are also made obvious by Miller et al. in view of Sirhan et al. reference C (see instant claims 1-3, 7-9, and 24-25). Miller et al. in view of Sirhan et al. reference C do not teach that the coronary stent is operably coupled to a catheter or that the therapeutic on the mid-region is different than that on the distal and proximal ends.

Sirhan et al. reference B teaches that an edge effect phenomenon is known to occur in patients that have had coronary stents deployed within them (see paragraph 19). Beyond the edges of the implanted stent severe stenosis often develops, thus the inventors developed a device that focuses drug delivery from the proximal and distal ends of a stent device that extends beyond the ends of the stent (see paragraph 22). The intermediate portion (mid-portion) of the stent between the distal and proximal regions is taught to have a therapeutic agent that is different and released with a different kinetic profile than that released from the ends (see paragraph 51; instant claims 10 and 21). These therapeutic agents are taught to be present in coating form on the stent (see paragraph 59). Particular therapeutic agents envisioned on the device, separately or in combination, include dexamethasone, rapamycin, rapamycin analogs, and prednisone (see paragraph 35; instant claims 3 and 15). Sirhan et al. reference B teaches that the stent is deployed via a balloon catheter (requiring that the stent and catheter be operably coupled) (see paragraph 48; instant claim 1). In addition, the presence of a biodegradable (bioerodible) rate controlling element (layer) that impedes the delivery of drug from the intermediate region (mid-portion) as compared to the ends to different degrees is also taught (see paragraphs 25 and 33; instant claim 9). Sirhan et

al. reference B also teaches that the therapeutic has a higher diffusion rate from the device at the ends than in the intermediate region (mid-portion) (see claim 7; instant claims 11 and 22). Sirhan et al. reference B does not explicitly teach a multi-layered configuration of drug containing coatings.

Since Sirhan et al. reference B and Miller et al. in view of Sirhan et al. reference C both teach drug eluting stents, it would have been obvious to one of ordinary skill to operably couple the stent of Miller et al. in view of Sirhan et al. reference C to a catheter so as to facilitate implantation. In addition, it also would have been obvious to configure the coating of Miller et al. in view of Sirhan et al. reference C in consideration of the stent edge effects as taught by Sirhan et al. reference B. This would yield a stent where the distal and proximal ends have at least two different drug coatings and two barrier (timing) coatings that alternate and can also have the intermediate (mid-region) portion with drug (different from that on the distal and proximal ends) coating and a barrier coating. This triumvirate of drugs would be obvious considering that Miller et al. in view of Sirhan et al. reference C and Sirhan et al. reference B teach a collection of drugs all known for the same purpose (treating restenosis) and their combination in and subsequent liberation from a stent would have been obvious (see "It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980) see MPEP 2144.06 and instant claims 8, 10, 26, and 28-29.)

From the teachings of Sirhan et al. reference B, the claimed differences in diffusion characteristics between the distal/proximal regions and intermediate region would follow from the combination of references. Further, since Miller et al. in view of Sirhan et al. reference C teach sequential delivery of drugs from their taught layered configuration, sequential delivery of the multiple drugs from the separate layers on the distal and proximal ends would also have been obvious.

Sirhan et al. reference B provides for the deployment of the stent made obvious by their teachings and those of Miller et al. in view of Sirhan et al. reference C to a vessel. Fischell et al. teach a coated stent where a biodegradable polymer containing barrier layer is on top of a drug layer to control its rate of release (see paragraph 49). They go on to teach that the thickness of the biodegradable is determined by its erosion properties (see paragraph 54). This indicates that the rate of erosion of a biodegradable barrier layer is directly related to the rate of release of the drug from its layer and that such polymer layers are actuated by erosion (see instant claims 1, 23, and 27). Since the polymers in each of the layers are taught to be biodegradable, they would be capable of controlling delivery of drug via erosion. So it then follows that the deployment of the device made obvious by Miller et al. in view of Sirhan et al. reference C and Sirhan et al. B that is configured to sequentially deliver the drugs from the distal and proximal ends would do so via the sequential actuation/erosion of overlying layers (e.g. erosion of top barrier allows delivery of first therapeutic; erosion of polymer in first therapeutic layer allows erosion of second barrier layer which then allows delivery of second therapeutic). Furthermore, instant claim 23 contains several active steps that

are physiological processes that occur due to the implantation of the claimed stent. No action by man is required or needed after deployment of the device to release the drug, erode the polymer of the first therapeutic coating, or actuate the first timing coating to release the second therapeutic. Fischell et al. demonstrate that the delivery mechanism claimed by the instant claims (e.g. instant claims 1 and 23) was known to occur in the claimed degradable barrier layer-drug layer configuration, which was made obvious by Miller et al. in view of Sirhan et al. reference C and Sirhan et al. reference B; thus the device of this modified reference would have necessarily functioned in this way upon implantation. Applicant has provided no teachings delineating a subpopulation of particular bioerodible polymers that are necessary to perform in the claimed capacity; therefore, it is the position of the examiner that even in the absence of the teachings of Fischell et al., the release of drug from the stent made obvious by Miller et al. in view of Sirhan et al. reference C and Sirhan et al. reference B would occur via the claimed method upon deployment to a vessel *in vivo*. Thus claims 1-3, 7-12, and 19-29 are obvious over Miller et al. in view of Sirhan et al. reference C and Sirhan et al. reference B and as evidenced by Fischell et al.

Claims 12 and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Miller et al. in view of Sirhan et al. reference C as applied to claims 12, 14-15, and 18-20 above, and further in view of Shanley et al. (US PGPub No. 2004/0249449).

Miller et al. in view of Sirhan et al. reference C make obvious a coronary stent with alternating barrier layers (timing coating) and therapeutic agent containing layers

that all contain bioerodible polymers and are arranged such that the distal and proximal ends have a plurality of each while the mid-portion has at least one of each. In addition, the claimed therapeutic agents, release kinetics (sequential release) and presence of bioerodible polymers in each layer are also made obvious by Miller et al. in view of Sirhan et al. reference C (see instant claim 12). Miller et al. in view of Sirhan et al. reference C do not explicitly teach that the therapeutic agents are released from their respective layers after the adjacent overlying timing coating has completely eroded.

Shanley et al. teach a medical device intended for delivery of therapeutic agents to blood vessels (see paragraph 41). In this device are regions that contain layers of different therapeutic agents such that different agents are released at different times (see paragraph 94). In a particular, Shanley et al. teach that the different layers are eroded sequentially so that the majority of a therapeutic in a first layer is released before the majority of a therapeutic agent in an underlying layer (see paragraph 94).

Since Shanley et al. teach sequential delivery of therapeutic agents from separate erodible layers via the sequential erosion of each layer, it would have been obvious to one of ordinary skill in the art to utilize such a phenomenon in the invention of Miller et al. in view of Sirhan et al. reference C since they also provide sequential release of therapeutic agents from separate bioerodible layers. Given that Miller et al. in view of Sirhan et al. reference C also teaches that their bioerodible barrier layers control the rate of release of therapeutic agents, the teachings of Shanley et al. would translate to the overlying barrier layer for a given therapeutic agent containing layer eroding before the therapeutic agent containing layer beneath it. Consequently, the barrier layer

would completely erode before its underlying therapeutic containing layer. In addition, it would then follow that in some embodiments encountered via routine experimentation some amount of therapeutic agent would remain in this underlying layer after the erosion of barrier layer and would be released by the time the therapeutic containing layer completely eroded. Therefore claims 12 and 31 are obvious over Miller et al. in view of Sirhan et al. reference C and Shanley et al.

Claims 1, 23, 30, and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Miller et al. in view of Sirhan et al. reference C and Sirhan et al. reference B and as evidenced by Fischell et al. as applied to claims 1-3, 7-12, and 19-29 above, and further in view of Shanley et al.

Miller et al. in view of Sirhan et al. reference C and Sirhan et al. reference B and as evidenced by Fischell et al. make obvious the products and methods as recited in claims 1 and 23 where the layered coating configuration provides sequential delivery of different therapeutic compounds one at a time. This modified reference does not explicitly teach that the therapeutic agents are released from their respective layers after the adjacent overlying timing coating has completely eroded.

Shanley et al. teach a medical device intended for delivery of therapeutic agents to blood vessels (see paragraph 41). In this device are regions that contain layers of different therapeutic agents such that different agents are released at different times (see paragraph 94). In a particular, Shanley et al. teach that the different layers are

eroded sequentially so that the majority of a therapeutic in a first layer is released before the majority of a therapeutic agent in an underlying layer (see paragraph 94).

Since Shanley et al. teach sequential delivery of therapeutic agents from separate erodible layers via the sequential erosion of each layer, it would have been obvious to one of ordinary skill in the art to utilize such a phenomenon in the invention of Miller et al. in view of Sirhan et al. reference C and Sirhan et al. reference B as evidenced by Fischell et al. since they also provide sequential release of therapeutic agents from separate bioerodible layers. Given that Miller et al. in view of Sirhan et al. reference C and Sirhan et al. reference B as evidenced by Fischell et al. also teaches that their bioerodible barrier layers control the rate of release of therapeutic agents, the teachings of Shanley et al. would translate to the overlying barrier layer for a given therapeutic agent containing layer eroding before the therapeutic agent containing layer beneath it. Consequently, the barrier layer would completely erode before its underlying therapeutic containing layer. In addition, it would then follow that in some embodiments encountered via routine experimentation some amount of therapeutic agent would remain in this underlying layer after the erosion of barrier layer and would be released by the time the therapeutic containing layer completely eroded. Therefore claims 1, 23, 30, and 32 are obvious over Miller et al. in view of Sirhan et al. reference C, Sirhan et al. reference B ., and Shanley et al. and as evidenced by Fischell et al.

Response to Arguments

Applicant's arguments filed January 27, 2010 have been fully considered but they are moot in light of the new grounds of rejection.

While an embodiment of Miller et al. did exist where the delivery of one drug was following by the delivery of a second drug, in light of the amendment to the claims, additional references are cited to address the "exclusive," "sequential" delivery now required.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The rejections and/or objections detailed above constitute the complete set presently being applied to the instant application.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CARALYNNE HELM whose telephone number is (571)270-3506. The examiner can normally be reached on Monday through Friday 9-5 (EDT).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert A. Wax can be reached on 571-272-0623. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Caralynne Helm/
Examiner, Art Unit 1615

/Robert A. Wax/
Supervisory Patent Examiner, Art Unit 1615